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(88) Date of publication of the international search report:
5 March 1998 (05.03.98)

(54) Title: OLIGONUCLEOTIDES FROM THE UNTRANSLATED REGIONS OF RIBONUCLEOTIDE REDUCTASE AND THEIR USE TO MODULATE CELL GROWTH

(57) Abstract

The invention relates to olignucleotides from the untranslated regions of housekeeping genes, and methods and compositions for modulating cell growth using same. Specifically it relates to the use of the untranslated regions (UTR) from housekeeping genes specifically the R1 and R2 components of ribonucleotide reductase UTR, for inhibiting tumor cell growth.

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INTERNATIONAL SEARCH REPORT

Intern. ,nal Application No
PCT/CA 97/00454

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C12N9/00 C12N15/11 C12N9/02 //C07K14/47

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C12N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	N. PAVLOFF ET AL.,: "Sequence analysis of the large and small subunits of human ribonucleotide reductase" DNA SEQUENCE, vol. 2, 1992, READING, GB, pages 227-234, XP002048232 see the whole document and specially figures 2 and 3 --- -/--	1,2,5,9, 17,24

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
3 December 1997	16.01.98

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Mateo Rosell, A.M.

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Inter onal Application No
PCT/CA 97/00454

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	N.J. PARKER ET AL.,: "Human M1 subunit of ribonucleotide reductase: cDNA sequence and expression in stimulated lymphocytes" NUCLEIC ACIDS RESEARCH, vol. 19, no. 13, 1991, OXFORD, GB, pages 3741-3741, XP002048233 see the whole document & EMBL/Genbank/DDBJ Databases Accession number no. X59543	1,2,9, 17,24
X	EMBL/Genbank/DDBJ Databases Accession number no. aa452273 Unpublished, created 11 June 1997 Hillier et al. "WashU-Merck EST Project 1997" XP002048834 see abstract	1,2,9, 17,24
X	EMBL/GenBank/DDBJ databases Accession number no. g07100 Unpublished, created 15 june 1995 Hudson et al., "The Whitehead Institute/MIT Center for Genome Research; Physically mapped ESTs" XP002048239 see abstract	1,5,9, 17,24
X	F.Y. CHEN ET AL.,: "Mammalian ribonucleotide reductase R1 mRNA stability under normal and phorbol ester stimulating conditions: involvement of a cis-trans interaction at the 3' untranslated region" THE EMBO JOURNAL, vol. 12, no. 10, 1993, OXFORD, GB, pages 3977-3986, XP002048234 cited in the application see the whole document and specially figures 6 and 7	1-4, 7-13, 17-19, 21-30
X	F.M. AMARA ET AL.,: "A novel transforming growth factor-beta 1 responsive cytoplasmic trans-acting factor binds selectively to the 3'-untranslated region of mammalian ribonucleotide reductase R2 mRNA: role in message stability" NUCLEIC ACIDS RESEARCH, vol. 21, no. 20, 1993, OXFORD, GB, pages 4803-4809, XP002048235 see the whole document and specially figure 3	1,2, 5-13,15, 17-19, 21-23, 25-30

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INTERNATIONAL SEARCH REPORT

Inter. nal Application No
PCT/CA 97/00454

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	T. SAEKI ET AL., : "Immunohistochemical detection of ribonucleotide reductase in human breast tumors" INTERNATIONAL JOURNAL OF ONCOLOGY, vol. 6, 1995, ATHENS, GR, pages 523-529, XP000608651 cited in the application see the whole document	20
Y	WO 94 21661 A (UNIV LELAND STANFORD JUNIOR) 29 September 1994 cited in the application see the whole document	1,8-10, 12, 14-16, 21-23, 27-30
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A	WO 95 02069 A (ISIS PHARMACEUTICALS INC) 19 January 1995 see abstract	1,8-10, 12, 14-16, 21-23, 27-29
A	WO 93 17125 A (BAYLOR COLLEGE MEDICINE ;ISIS PHARMACEUTICALS INC) 2 September 1993 see abstract	1,8-10, 12, 14-16, 21-23, 27-29
A	EP 0 383 190 A (BIO MEGA INC) 22 August 1990 see the whole document	14,16
A	H. KIJIMA ET AL., : "Therapeutic applications of ribozymes" PHARMACEUTICAL THERAPEUTICS, vol. 68, no. 2, 1995, AMSTERDAM, NL, pages 247-267, XP000612090 see the whole document	9

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INTERNATIONAL SEARCH REPORT

Inter ɔnal Application No
PCT/CA 97/00454

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	EP 0 726 277 A (KYOWA HAKKO KOGYO KK) 14 August 1996 see the whole document	20
P,X	H. FAN ET AL.: "Suppression of malignancy by the 3' untranslated regions of ribonucleotide reductase R1 and R2 messenger RNAs" CANCER RESEARCH, vol. 56, no. 19, 1 October 1996, PHILADELPHIA, PA, US, pages 4366-4369, XP002048238 see the whole document, specially tables 1 and 2	2,10,11, 14,16, 17, 25-28,30

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA 97/00454

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

see FURTHER INFORMATION sheet PCT/ISA/210

2. [X] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/CA 97/00454

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

Claims Nos.: 1,14,16,22,23,27-30

because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

Claims 1,14,16,22,23, 27 and 29 to 'housekeeping gene(s)'. The term 'housekeeping' is too broad (Art. 6 PCT and rule 33.3 (b) 3.7 from PCT Guidelines).
According to the description (see page 8), this term is used in the application refering to 'genes/functions/activities that are required by most cycling cells and critically linked to general cell metabolism'. Examples of housekeeping genes are given in Table 3 (page 28). This list is very extensive, making a complete search impossible. For economical reasons, the search was limited to real examples provided by the applicant, i.e. . SEQ.ID.N. 1,2, 6-49 which correspond to the complete sequence or fragments (20 mer oligonucleotides) of the human ribonucleotide reductase.

Remark : Although claims 27,28,30 are directed to a method of treatment of the human/animal body , the search has been carried out and based on the alleged effects of the compound/composition.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inten nal Application No
PCT/CA 97/00454

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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